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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/079,075	02/19/2002	Ronald C. Montelaro	A34001-A/072396.0222	4545

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EXAMINER	
LIU, SAMUEL W	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/079,075	MONTELARO ET AL.	
	Examiner	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *20 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 8-41* is/are pending in the application.

4a) Of the above claim(s) *none* is/are withdrawn from consideration.

5)☒ Claim(s) *1, 8-28 and 34-41* is/are allowed.

6)☒ Claim(s) *29-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1 and 8-41 are pending.

Applicants' amendment filed 20 January 2004, which amends claim 1, 27-34, 38 and 40, and cancels claims 42-65 has been entered. Also, applicants' request for extension of time of three months has been entered. Note that claims 2-7 are canceled by applicants' amendment filed 13 December 2002.

The following Office action is applicable to the pending claims 1 and 8-41.

Please note that grounds of objection and/or rejection not explicitly restated and/or set forth below are withdrawn.

The following is a new ground rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated antimicrobial peptides of SEQ ID NOs: 4-12. The specification does not reasonably provide enablement for any isolated and purified analogs of lentiviral lytic peptide-1 (LLP-1). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The application disclosure and claims have been compared per the factors indicated in the decision *in re* Wands 8 USPQ2d 1400, 1400 (Fed. Cir. 1998). These factors are considered when determining whether there is sufficient evidence to support a description that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. The factors include but not limited to: 1) the nature of the invention; 2) the breath of the claims; 3) the predictability or unpredictability of the art; 4) the amount of direction or guidance presented; 5) the presence or absence of working examples; 6) the quantity of experimentation necessary; 7) the relative skill of those skilled in the art.

Each factor applicable is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

(1) The scope of the claims/(2) The nature of the invention:

Claims 29-34 set forth the isolated LLP-1 peptide analog. Such the claim language broadly encompass a large number of peptide variant as the specification sets forth that the analog is a peptide which contains mutations, e.g., substitution, rearrangements, deletion, additions an/or chemical modifications (see [0037]). The specification only provide working examples as to the structural features of the parental peptides e.g., SEQ ID NOs: 5 and 6 (see example 1), antibacterial activity of SEQ ID NOs: 1-3 peptides (see examples 2-3), and solid immobilization and its biological application of SEQ ID NO:2 (see example 4). Of these examples, SEQ ID NOs:1-3 are NOT subject matters of the current invention. Thus, the specification does not appear to provide working example as to biological activity of any LLP-1 analogs thereof. In addition, the specification is silent in teaching core structure or motif(s) which plays critical role in antimicrobial activities of the analogs. Thus, the specification provide

insufficient guidance and no working examples as to how to make and use the peptide analogs of parent peptides of SEQ ID NOs: 4-12 with regard to their antimicrobial or/and antiviral applications. The skilled artisan, therefore, cannot envision all the contemplated LLP-1 analog possibilities which are structurally and/or functionally divergent from unmodified LLP-1 peptides, and would not know how to make (e.g., how to make chemically-modified analog) and use the LLP-1 analog(s) to immobilized the said peptides in a solid surface for antimicrobial application while exhibit minimal toxicity to subject cells *in vitro* and *in vivo* (see abstract). The current disclosure is not enabling any LLP-1 analog peptides in said applications. Therefore, the scope of claims is outside the bounds of the enablement and would have resulted in the necessity of undue experimentation.

(3) The unpredictability of the art:

The claimed invention is directed to a large number of the LLP-1 peptide analogs, which include any mutants (genetically or/and chemically generated). The specification provides insufficient direction and teaching as to how to chemically modify the LLP-1 peptide from any one of SEQ ID NOs: 4-12, e.g., modified one or more amino acid residue in order to covalently attach the analog peptide to a solid surface. Since none of SEQ ID NOs:4-12 has cysteine residue, the said chemical modification must occur in any functional/active groups (e.g., hydroxyl or amine group(s)) of amino acid residue(s). Yet, the specification fails to teach this modification. Honig *et al.* teach that the amino acid residues of a protein that can tolerate structural change (*e.g.*, mutations: conservative substitution or no substitution, addition or deletion) which are critical to maintain the protein's structure will require guidance (see *Honig, B.* (1999) *J. Mol. Biol.* 293, 283-293). Kalia V. et al. teach (*J. Virology* (2003) 77, 3634-3646)

that the LLP-1 mutants exhibit about 80% decrease in biological activities, e.g., fusogenicity (see abstract and Figure 2). Also, Tencza, A. B. et al. teach that a single mutation in LLP-1 peptide effectively abolish its biological activity (see page 5200, the reference cited in the IDS filed 19 February 2002 by applicants). These suggest that mutations introduced into the LLP-1 peptides may produce unpredictable results.

Given the lack of sufficient guidance and working examples, predicting what changes can be made to the amino acid sequence of the parent peptides of SEQ ID NOs: 4-12 that after truncation or deletion, substitution or/and other chemical modification will retain the same structure (e.g., amphipathic alpha-helix) and antimicrobial activities as the parent (unmodified) peptides is unpredictable. Because the specification fails to teach how to chemically modify peptides, the skilled artisan cannot practice the invention without undue experimentation.

(4) The state of the prior art:

The general knowledge and level of skilled in the art do not supplement the omitted description because specific, not general, guidance is what is needed. As stated above, the current claim language "peptide analog" represents a genus encompassing numerous variants of the LLP-1 peptides (especially those mutants resulted from *chemical modification* in combination with genetic mutations). Because the genus is highly variant, the specification needs to provide sufficient guidance to be considered enabling.

(5) The quantity of experimentation necessary:

In the absence of working examples with regard to the genus stated above, unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue trials and errors to practice the claimed invention. The quantity

of experimentation would be large and unpredictable (see the above statement). One skilled in the art would be required to carry out an undue experimentation for finding out which kind chemical modification in combined with genetic mutagenesis (e.g., deletion, additions, substitution or trancation) are suitable for producing an amphipathic alpha helix peptide having antimicrobial activity comparable with unmodified peptide.

(6) The relative skill of those in the art:

The general knowledge and level of skill in the art do not supplement the omitted description with respect to a massive number of variant sequences of peptide. In view of the preceding factors (1-5), the level of skill in this art is high and requires at least a molecular biologist with several years of experience in mutagenesis, peptide chemistry and protein engineering as well as knowledge in microbiology, virology, peptide chemistry, pathology and pharmacology. Yet, even with a level of skill in the art as those mentioned in precedence, predictability of the results is still highly variable. An unduly level of skill is needed for the skilled artisan in order to identify the useful LLP-1 analog compound, which has potent antimicrobial or/and antiviral ability with or without being immobilized to a solid surface while has minimal cytotoxicity to the subject eukaryotic cells.

In consideration of each of factors stated above, absent factual data to the contrary, the amount and level of experimentation needed is undue.

Provisional Rejection, 35 U.S.C. 101, Double Patenting

The provisional double patenting rejection is withdrawn because applicants abandoned application No. 09785058, to which the current invention is compared.

Conclusion

Claims 29-33 are not allowed; claims 1, 8-28 and 34-41 are free from prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

Samuel Wei Liu, Ph.D.

April 5, 2004